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Regular Article

Early life health adversity and internalizing disorders in the transition from adolescence to adulthood

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Abstract

Early life adversity (ELA) and youth chronic health conditions have been examined as separate contributors to psychopathology. However, little work has specifically examined early life *health* adversity (ELHA) and its association with risk for internalizing disorders. This study seeks to examine the relationship between ELHA and internalizing disorders across adolescence. A sample of 705 Australian mother–youth dyads participated in a prospective longitudinal study. Mothers reported child health indicators at youth ages three-to-four days, six months, and five years and completed a psychiatric interview at 15 years. Youth completed a psychiatric interview, as well as measures of current health status, at age 20. ELHA was positively associated with both youth anxiety and depressive disorders from ages 15 to 20. When independently accounting for the role of (a) current health status and (b) exposure to traditionally conceptualized forms of ELA, these findings remained statistically significant for anxiety but not depressive disorders. ELHA interacted with maternal depression, such that ELHA was only associated with youth depressive disorders in cases where mothers themselves had experienced depression. Routine mental health screenings may be warranted for youth who experience ELHA and their mothers. Pediatric primary care may be an ideal setting for implementing prevention and intervention efforts.

Keywords: adolescence; anxiety; depression; early life health adversity; pediatrics

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Introduction

Youth who experience early life adversity (ELA) are at heightened risk for developing subsequent psychiatric disorders. In fact, data from large, nationally representative samples of adolescents ($N = 6483$; McLaughlin et al., 2012) and adults ($N = 9282$; Green et al., 2010) as well as a World Health Organization (WHO) study of 21 countries ($N = 51{,}945$; Kessler et al., 2010) suggest that ELA contributes to approximately 30 percent of all mental health disorders. A large body of evidence indicates that youth who are exposed to ELA go on to display elevated rates of both internalizing (i.e., anxiety and depressive) and externalizing (i.e., disruptive behavior and substance use) disorders (Aafjes-van Doorn, 2020; Green et al., 2010; Healy et al., 2021; Kessler et al., 2010; McLaughlin et al., 2012). Although precise definitions of ELA vary by study, measures typically assess various forms of maltreatment, socioeconomic disadvantage, and/or violence exposure (Gee, 2021). For instance, the seminal Adverse Childhood Experience (ACE) Study (Felitti et al., 1998) examined seven early life adversities, including physical, psychological, or sexual abuse; maternal exposure to violence; and living with individuals with mental illness or suicidality, substance misuse, or history of imprisonment. Likewise, the WHO World Mental Health Survey assessed 12 early life adversities, including three types of maltreatment (physical abuse, sexual abuse, and neglect), three types of interpersonal loss (parental death, parental divorce, and other separation from parents), four types of parental maladjustment (mental illness, substance misuse, criminality, and violence), and two other adversities (life-threatening physical illness, family economic adversity; Kessler et al., 2010). Central to each of these adversities are elements of unpredictability (Ellis et al., 2009), uncontrollability (Cohodes et al., 2021), threat, and/or deprivation (Sheridan & McLaughlin, 2014). Decades of research suggest that adversities characterized by high degrees of unpredictability and uncontrollability are associated with poor mental health outcomes (Baram et al., 2012; Gee, 2021, McLaughlin et al., 2021, Seligman et al., 1971; Weinberg & Levine, 1980). More recently, scholars have sought to classify early life adverse experiences – and their subsequently associated mental health outcomes – along the dimensions of threat (i.e., significant potential for harm) and deprivation (i.e., absence of an expected environmental input; Gee, 2021; Sheridan & McLaughlin, 2014). However, surprisingly little research has examined early life *health* adversity, a form of ELA that is not only prevalent but also potentially characterized by unpredictability, uncontrollability, threat, and deprivation.

Youth with a range of physical health conditions are at risk for mental health problems, both in childhood and across the lifespan (Adams et al., 2019; Secinti et al., 2017; Berkelbach van der Sprenkel et al., 2022). A recent nationally representative cohort study concluded that youth with chronic physical conditions (e.g., asthma, diabetes, and migraine) are at approximately 50% greater risk for psychiatric disorders than those without physical

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conditions, which is partially explained by activity limitations (Adams et al., 2019). In terms of long-term consequences, a recent systematic review and meta-analysis revealed that children who experience chronic physical illnesses are more likely to have anxiety and depressive disorders in adulthood (Secinti et al., 2017). Furthermore, data from the United States Health and Retirement Study indicated that childhood chronic illness is associated with major depression in adults over 50 years of age (Bergmans & Smith, 2021), suggesting that the mental health effects of childhood chronic illness are themselves chronic. In this study, more than half of this relationship was mediated by childhood mental health status, emphasizing the importance of early intervention and prevention efforts. Notably, the negative mental health outcomes associated with childhood medical conditions are not limited to lifelong serious, debilitating chronic illnesses. For instance, one study found that children with ongoing ear infections or hearing problems at four-to-five years of age were more likely to evince psychosocial difficulties at ten-to-eleven years of age (Hogan et al., 2014). Moreover, in a population-based Australian cohort study of 91,635 youth, children who were hospitalized for infection between birth and four years of age were more likely to develop a psychiatric disorder between five and 13 years of age (Green et al., 2021). Although research to-date has largely examined the relationship between individual physical health conditions and/or mental health outcomes, putting this work together broadly suggests that youth who experience an array of physical health problems are at heightened risk for an array of subsequent mental health problems – particularly anxiety and depressive disorders – that last into adolescence and adulthood (Secinti et al., 2017). The presently theorized relationship between early life health adversity and subsequent internalizing disorders may be explained by several biopsychosocial mechanisms. The traditional ELA literature has identified mechanisms across several levels of analysis, such as neuroendocrine and immune system functioning, caregiving behaviors, and cognitive patterns, whereby early adversity may increase risk for psychiatric disorders (Nelson et al., 2020). While general research on mental health problems in youth with medical conditions has tended to focus on affective, behavioral, and cognitive mechanisms, biological mechanisms have recently received growing attention in certain conditions, such as pain and asthma (Rosa et al, 2018; Vinall et al., 2016). It is easy to imagine how early life health adversity could, for example, lead to maladaptive physiological alterations, cognitive biases, or attachment styles, all of which could set the stage for internalizing disorders.

An ELA framework emphasizes the importance of developmental timing. Adverse experiences that occur during sensitive developmental periods, such as infancy or early childhood, may exert particularly potent effects due to the developing brain being highly sensitive to environmental inputs at this time (Gee, 2021). To-date, however, scant research has examined the unique long-lasting effects of health adversity experienced within the first few years of life (Adams et al., 2019; De Young et al., 2021; Secinti et al., 2017). Aside from early life, recent research highlights the importance of adolescence as another sensitive period, through which puberty opens a later window of increased plasticity (DePasquale et al., 2019). This heightened plasticity may increase adolescent susceptibility to negative environmental inputs, contributing to increased risk for mental health disorders during this time (WHO, 2012). The peak age of onset of several anxiety and depressive disorders occurs during adolescence, and adolescent internalizing disorders are associated with recurrent psychopathology, suicidality, and psychosocial difficulties across the lifespan (McLaughlin & King, 2015). However, not all youth who are exposed to ELA, or to a range of pediatric medical problems, subsequently develop psychopathology. In fact, the pioneering scholars in developmental psychopathology and developmental resilience science (Masten & Cicchetti, 2016; Masten, 2024) suggest that risk and resilience be studied in tandem. In order to best identify youth at greatest risk and inform preventative and intervention efforts, it is important to (a) test the direct association between early life health adversity and mental health outcomes in adolescence and young adulthood and (b) explore factors that attenuate or exacerbate this relationship.

In previous studies with the current cohort, our colleagues have collectively examined a range of early life health problems using a composite of health indicators (including but not limited to chronic illness) from birth up to age five. Poor early childhood physical health (even when chronic illness was removed from the composite) predicted health-related stress and social difficulties at age 20, which in turn predicted depressive symptoms at age 25 (Raposa et al., 2014). Importantly, this cohort is a sample with a high prevalence of maternal depression, which gives us the unique opportunity to explore maternal depression as a potential moderator in the relationship between early life health adversity and internalizing disorders in adolescence. It is possible that maternal depression interacts with early life health adversity in a diathesis-stress (Monroe & Simons, 1991) fashion, such that youth who are exposed to maternal depression demonstrate heightened susceptibility to the long-lasting effects of health problems in early life.

Theory and research to-date suggest that social relationships may serve as protective factors for youth who experience early life health adversity. For instance, quality family relationships, close friendships, and larger peer network relationships may also promote positive mental health outcomes among youth who experience early life health adversity. Growing literature on the social buffering of stress describes how the presence and availability of supportive social figures can decrease the activity of stress-mediating physiological systems in an individual, thus reducing the deleterious effects of stress exposure (Gunnar, 2017). Supportive family relationships may be particularly important in youth who experience early life health adversity, as such adversity may cause significant stress on the entire family unit (Cousino & Hazen, 2013; Grunberg et al., 2023; Kazak, 1989). Parental support and family cohesion have received great attention within the pediatric psychology literature, in part because medical management may largely fall in the hands of the caregivers (Hilliard et al., 2015). As children transition to adolescence and young adulthood, peers play an increasingly powerful role in psychosocial adjustment. Given that pediatric medical conditions may exert unique effects on social competence and relationships, and that peer relationships may exert unique effects on health behaviors, it is important to examine the impact of both close friendships and the larger peer networks in youth exposed to early life health adversity (Helgeson & Holmbeck, 2014). Examining the potential protective role of social relationships in early adolescence is particularly important given that this timepoint parallels or precedes the peak onset of internalizing disorders. While much literature focuses on the enduring negative effects of early adversity, studying potential modifiable social factors that promote resilience to psychopathology will inform intervention and prevention efforts across development.

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Although previous research suggests that youth who are exposed to early life health adversity are at-risk for depression by early adulthood, no previous research, to our knowledge, has examined the relationship between early health problems and subsequent anxiety disorders. Additionally, it is unknown whether early life health adversity adds predictive value when accounting for more traditionally conceptualized forms of childhood adversity, or current health status. Previous work with the current cohort has focused on risk factors for psychopathology, yet it is important to also examine the extent to which modifiable social factors in adolescence may protect youth who experience early life health adversity from developing internalizing disorders.

The current study

In the current study, we prospectively examined the relationship between early life health adversity and internalizing disorders present in the transition from adolescence to adulthood. Our first aim was to examine the main effects of early life health adversity on internalizing disorders across adolescence. We hypothesized that youth with adverse health experiences by five years of age would be more likely to meet criteria for an anxiety or depressive disorder between 15 and 20 years of age. Furthermore, we hypothesized that early life health adversity would continue to add predictive value after independently accounting for (a) more traditionally conceptualized forms of ELA and (b) current health status at age 20. Our second aim was to examine key social relationships at age 15 that may serve as protective factors. We hypothesized that the relationship between early life health adversity and internalizing disorders across adolescence would be attenuated among youth with high-quality family relationships, close friendships, and social lives. Given the unique opportunity to prospectively study the relationship between early life health adversity and subsequent internalizing disorders in a large sample with a high prevalence of maternal depression, our third and final exploratory aim was to examine youth biological sex and maternal depression as potential moderators of the association between early life health adversity and internalizing disorders later in development.

Method

Participants and procedure

Participants included 705 mother–youth dyads who participated in a prospective, longitudinal study from birth to youth age 20 years. This sample was drawn from a subset of the Mater-University Study of Pregnancy (MUSP), which initially followed a birth cohort of more than 7,000 women and offspring in Brisbane, Australia (Keeping et al., 1989). All children were born in a public (free) hospital in Brisbane, with the sample being somewhat skewed toward low-income families. Mothers were recruited in pregnancy, and dyads were followed at birth and at youth ages six months and five years. Depression questionnaires were administered to mothers during pregnancy and at three additional times (see Hammen & Brennan, 2001 for details). At youth age 15, dyads from the larger cohort were selected to create a sample enriched for maternal depression, including mothers with a wide range of depressive symptom severity and chronicity levels throughout their youth's life, as well as non-depressed controls. Of the 991 dyads targeted for continued study participation, 815 (82.24%) participated at age 15. These high-risk youth did not differ statistically significantly from the original birth cohort in terms of biological sex, maternal education, or family income. Of those 815 youth, 705 (86.50%) participated at age 20. Compared to those who participated, those who did not participate at age 20 were more likely to be male, have lower maternal education at time of pregnancy, and have lower family income at age 15 (Keenan Miller et al., 2007; Raposa et al., 2014).

The current sample includes all youth who participated in the age 20 interview. Youth were split approximately evenly by biological sex, with 342 (48.5%) males and 363 (51.5%) females. Youth were primarily White (91.3%), with the remaining participants having Asian (4.7%), Maori/Islander (2.0%), and Aboriginal (2.0%) ethnic backgrounds. During pregnancy, mothers were an average age of 25.52 years ($SD = 5.08$). Family income indicated that participants were predominately lower middle to middle class.

During pregnancy, approximately three-to-four days after delivery, at youth age six months, and at youth age five years, mothers completed questionnaires related to demographic information, youth physical health, and youth adversity exposure. When youth were 15 and 20 years of age, mothers and youth completed a variety of questionnaires and interviews to assess psychological well-being, social functioning, and physical health. Time points were chosen to reflect sensitive developmental periods and to capitalize on the prospective longitudinal study design. In other words, adversity measures were isolated to the perinatal period through five years, in line with a plethora of literature demonstrating the long-lasting effects of adversity within the first few years of life (Gee, 2021). Anxiety and depressive disorders were assessed at age 20, with the diagnostic interview covering ages 15 through 20, given the heightened risk for the emergence of internalizing disorders during this period (McLaughlin & King, 2015). Maternal depression and adolescent social functioning were assessed at age 15 to ensure that these potential risk or protective factors temporally preceded the mental health outcomes of interest.

Study visits were completed at home or in another convenient location, interviews were conducted by trained masters level graduate students, and participants were compensated for their time. Mothers provided informed consent at each time point. Youth provided assent at age 15 and informed consent at age 20. All waves of this study were approved by the University of Queensland; the ages 15 and 20 waves were additionally approved by the University of California, Los Angeles and Emory University Institutional Review Boards.

Measures

Demographics, early life adversity, and maternal mental health

Demographics

Three-to-four days after giving birth, mothers reported the highest level of parental education (of either parent, in two-parent households) and current family income. Education and income were each categorized into seven categorical levels, with "1" representing the lowest education or income and "7" representing the highest education level or income bracket. Mothers also indicated the biological sex and ethnicity of their child.

Early life health adversity

Consistent with previous research in this cohort (Raposa et al., 2014), a composite of physical health was used to represent health problems from birth through five years of age. It is well established that the first few years of life represent a sensitive developmental

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period, whereby the effects of adversity may be particularly salient (Koss & Gunnar, 2018). Whereas studies examining early life health problems tend to focus on specific types of adverse health experiences and their association with later internalizing problems (e.g., prematurity and asthma), a composite or count variable was chosen to represent a range of acute and chronic problems experienced throughout the first five years of life and examine their cumulative effects (Larsen et al., 2010; Ortega et al., 2002). Although medical records are considered the "gold standard" for health research, previous studies have documented high validity when comparing parent reports and medical records with respect to early life hospitalizations and emergency department usage (D'Souza- Vazirani et al., 2005) and atopic symptoms and infections (Vissing et al., 2012). Furthermore, it has been suggested that parental healthcare and healthcare utilization reports are most accurate in young children (D'Souza- Vazirani et al., 2005; Kosa et al., 1967), which is the focus of the current study. This composite represents a count score composed of the following six indicators, all of which were coded dichotomously to create a count of adversities ranging from 0 to 6.

Postnatal health problems

Three-to-four days after birth, mothers were asked whether their infant had experienced any medical problems (e.g., prematurity, respiratory problems, and jaundice) during or immediately following birth. They were given the following response categories: (a) no, did not happen; (b) yes, but it was not a problem; (c) yes, it was a moderate problem; and (d) yes, it was a major problem. Responses indicating "moderate" or "major" neonatal medical problems were coded as child having a postnatal health problem.

Health problems in infancy

Six months following birth, mothers reported whether their child had experienced a variety of health difficulties (e.g., diarrhea or constipation, feeding problems, and skin problems). One point was given for each health difficulty that the mother endorsed as occurring several times per month or more, creating a sum score of infant health difficulties. Sum scores in the top third of the sample were then coded as child having health problems in infancy. This cutoff was chosen to be consistent across measures and with previous research with this sample (Hazel et al., 2008; Raposa et al., 2014), as well as to obtain sufficient variability for meaningful analyses. Throughout both the early life health and general adversity indices, the 33rd percentile was selected as a cutoff point to indicate the greatest adversity.

Healthcare utilization in infancy

Six months following birth, mothers reported on the frequency of seeking healthcare services for their child. Responses in the top third of the sample, in terms of frequencies, were coded as child high healthcare utilization in infancy.

Multiple hospitalizations by five years

At five years of age, mothers indicated how many times since birth their child had experienced a hospitalization; children with more than one hospitalization were coded as child multiple hospitalizations.

Physical limitations at five years

At five years of age, mothers were asked whether their child had physical limitations that impacted daily activities. Endorsement of this item was coded as child physical health limitations.

Chronic illness by five years

At five years of age, mothers indicated whether their child had experienced any chronic medical conditions (e.g., asthma, epilepsy, and diabetes); any endorsement was coded as child chronic illness.

General early life adversity

To examine the role of early life health adversity above and beyond more traditionally conceptualized forms of ELA, a composite of general ELA was created. This composite has been previously used with this sample (Hazel et al., 2008; Smearman et al., 2015) and reflects a range of adverse childhood experiences that have been associated with subsequent internalizing problems, including financial hardship (e.g., Najman et al., 2010), maternal stressful life events (e.g., Kingsbury et al., 2016), and both parental discord and separation from partners (e.g., Hayatbakhsh et al., 2013). While the original index consisted of six items, serious childhood illness and maternal psychopathology were omitted given their inclusion as variables of interest in the current study. This composite included the following four indicators, all of which were coded dichotomously to create a general ELA scale ranging from 0 to 4.

Financial hardship

During pregnancy and at child ages six months and five years, mothers reported total household income. The mean of these three time points was calculated to represent early childhood family income. Values in the bottom third of the sample (at or below Australian $10,399 in the period 1981–1983) were coded as experiencing financial hardship.

Maternal stressful life events

During pregnancy and at child age six months, mothers completed a checklist consisting of nine health (of self), interpersonal, and occupational problems across the previous six months, effectively capturing stressful life events during the prenatal and early postnatal periods. The numbers of events at each time point were highly correlated ($r = 0.59$) and were added together to create a single variable representing perinatal stressful life events. Values in the top third of the sample were coded as experiencing elevated maternal stressful life events.

Parental discord

During pregnancy and at birth, six months, and five years, mothers completed the satisfaction scale of the Dyadic Adjustment Scale (Spanier, 1976) to assess relationship satisfaction with their romantic partners. The mean of this eight-item scale was calculated across time points (alphas were 0.85 – 0.97). Values in the bottom third of the sample were coded as experiencing relationship discord.

Separation from partners

At child age five years, mothers were asked whether they had changed partners, separated, or been divorced over the last five years. An affirmative answer to this question was coded as child experiencing parental partner separation.

Maternal depression

At 15 years of age, maternal depressive disorders (major depressive disorder and dysthymic disorder) were assessed using the Structured Clinical Interview for DSM-IV (SCID-IV; First et al., 1995). To determine interrater reliability, independent judges, who were blind to the initial diagnoses, reviewed and rated 33 cases.

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Kappas for depressive disorders were 1.00 (current) and 0.79 (past). Any current or past history of maternal depression was coded as maternal depression and included as a covariate in all analyses.

Internalizing disorders and physical health in adolescence and early adulthood

Youth internalizing disorders

At 20 years of age, youth internalizing disorders were assessed using the Structured Clinical Interview for DSM-IV (SCID-IV; First et al., 1995). This semi-structured interview assessed psychiatric disorders between the 15-year and 20-year visit. For the current study, DSM-IV anxiety (panic disorder, agoraphobia, social phobia, obsessive–compulsive disorder, generalized anxiety disorder, and posttraumatic stress disorder) and depressive disorders (major depressive disorder and dysthymic disorder) were examined. A diagnosis of any one depressive disorder was coded as depressive disorder present in the transition from adolescence to adulthood; a diagnosis of any one anxiety disorder was coded as anxiety disorder present during this developmental transition. To determine interrater reliability, independent judges, who were blind to the initial diagnoses, reviewed and rated 55 cases. Kappas were 0.83 (current) and 0.89 (past) for depressive disorders and 0.94 (current) and 0.89 (past) for anxiety disorders.

Early adulthood current health status

At age 20 years, youth completed the Health of Self domain of the UCLA Life Stress Interview (LSI; Hammen, 1991) to assess general health over the previous six months. This gold-standard, semi-structured, face-to-face interview assessed youth's experiences of acute stress over the previous 12 months and chronic stress over the previous six months. For chronic stress domains, including Health of Self, each interviewer used a five-point-scale to assign an objective rating to indicate the level of functioning, with one representing exceptional functioning and five indicating extreme adversity. To assess health, interviewers used general questions, specific probes, and behavioral anchors to comprehensively assess any health conditions and associated duration, treatment, care required, and disability. Scores were reduced if participants smoke, drank excessively, did not pursue physical exercise, or were significantly overweight. Health quality was rated on a five-point scale, with one indicating exceptionally good health and five indicating a life-threatening health problem. This measure has been validated with other indices of health problems (Keenan-Miller et al., 2007), and interrater reliability was high in this sample (0.77).

Social relationships in adolescence (Age 15)

Family relationship quality

Youth completed the Family Relationships domain of the LSI (Hammen, 1991). Youth are asked "how's your relationship with your family going?" and probed for information about closeness, confiding, communication, trust, acceptance, frequency and nature of arguments, conflict resolution, availability, and dependability. The interviewer assigns family relationships an objective rating, with one representing exceptional quality relationships with all family members and five indicating poor relationship quality and no family members to turn to. Interrater reliability was high, with an interclass correlation of 0.83.

Close friendship quality

Youth completed the Close Friendships domain of the LSI. Youth are asked "Do you have close friends? How have these relationships been going?" and are probed for information about closeness, trust, location, dependability, and arguments. The interviewer assigns close friendships an objective rating, with one representing the presence of an exceptionally high quality, close, confiding friendship, and five indicating the absence of a close, confiding friendship. Interrater reliability was sufficient, with an interclass correlations of 0.72.

Social life quality

Youth completed the Social Life domain of the LSI. Youth are asked "How frequently do you do social activities?" and are probed for details regarding peer relationships and activities. The interviewer assigns social life an objective rating, with one indicating exceptional social life and five indicating severe social problems. Interrater reliability was sufficient, with an interclass correlation of 0.75.

Data analytic plan

Preliminary analyses

All analyses were conducted using IBM SPSS Statistics, version 28. First, we computed the early life health adversity and general ELA composite variables. We then conducted preliminary analyses to assess sample characteristics, normality, and multicollinearity. All analyses included the following covariates, which we selected *a priori*: youth biological sex, maternal diagnoses of depressive disorders through youth age 15 years, and maternal education during pregnancy. Missing data occurred in less than two percent of the sample; in the few cases of missing data (range = 4 to 12 cases of 705), listwise deletion was used in analyses. For moderation analyses, interaction terms were mean-centered.

Primary analyses

Hypothesis 1

We first tested the hypothesis that youth who experienced health adversity by five years of age would be more likely to meet criteria for an anxiety or depressive disorder between 15 and 20 years of age. We performed separate logistic regressions for anxiety and depressive disorders due to the bias towards maternal depression in this sample, the conceptual differences between the constructs, and the relative paucity of literature on youth health problems and anxiety, compared to depression. After assessing main effects, we then examined the predictive value of early life health adversity after independently accounting for (a) more traditionally conceptualized forms of ELA and (b) current health status at age 20. We repeated logistic regressions while adding a term in the second block to represent each of these additional variables.

Hypothesis 2

We next tested the hypothesis that the relationship between early life health adversity and internalizing disorders would be attenuated in youth who displayed higher quality social relationships at 15 years of age. For each potentially protective social relationship (family relationship quality, close friendships, and social life), we repeated the logistic regressions examining main effects while adding a term in the second block to represent the interaction between early life health adversity and each potential protective social factor. If the interaction term statistically significantly predicted anxiety and depressive disorders in

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adolescence, we planned to probe the direction of the interaction using SPSS MODPROBE.

Hypothesis 3

As exploratory hypotheses, we then examined variables that may moderate the relationship between early life health adversity and subsequent internalizing disorders in a diathesis-stress fashion. We repeated the main effect analyses while adding a term in the second block to represent the interaction between early life health adversity and (a) biological sex and (b) maternal depression. If the interaction term statistically significantly predicted anxiety and depressive disorders in adolescence, we planned to assess the direction of the interaction by repeating the analyses using each dichotomous values (e.g., running the same regression separately for males versus females and absence versus presence of maternal depression).

Results

Demographic and descriptive characteristics of our sample are presented in Table 1. Correlations between key study variables are presented in Table 2. As expected with this sample, prevalence of maternal depression was high; 41.8% of mothers met criteria for a depressive disorder by offspring age 15. There was sufficient variability within both the early life health adversity and general ELA indices, with youth representing the full continuum of adverse health and general experiences from birth through age five; these indices were statistically significantly correlated, albeit to a small degree ($r = .197$, $p < .001$). Early life health adversity was also statistically significantly correlated with current health status at age 20, but also to a small magnitude ($r = .137$, $p < .001$). There was sufficient variability in the presence of offspring internalizing disorders between 15 and 20 years of age. Specifically, 105 youth (14.89%) met criteria for only a depressive disorder, 82 youth (11.63%) met criteria for only an anxiety disorder, 86 youth (12.20%) met criteria for both anxiety and depressive disorders, and 432 youth (61.28%) did not meet criteria for either type of disorder. Potential social protective factors were all statistically significantly correlated ($rs = .159$, $.205$, $.509$; $ps < .001$) and represented nearly the full range of variability.

Our first hypothesis was that youth with adverse health experiences by five years of age would be more likely to meet criteria for a depressive or anxiety disorder in adolescence and early adulthood. Results for this hypothesis are presented in Tables 3 (depressive disorders) and 4 (anxiety disorders). Consistent with our hypothesis, early life health adversity was statistically significantly associated with both depressive and anxiety disorders in offspring between 15 and 20 years of age. For each additional early life health adversity experienced, youth were 1.17 times as likely to be diagnosed with a depressive disorder and 1.18 times as likely to be diagnosed with an anxiety disorder between 15 and 20 years of age. In other words, compared to youth exposed to no health adversities, youth exposed to all six early life health adversities were 2.57 times as likely to be diagnosed with a depressive disorder and 2.70 times as likely to be diagnosed with an anxiety disorder between 15 and 20 years of age. However, findings for depressive and anxiety disorder outcomes diverged when controlling for (a) more traditionally conceptualized forms of ELA and (b) current health status at age 20. After accounting for each of these factors independently, early life health adversity was no longer statistically significantly associated with offspring depressive disorders. On the other hand, even after accounting for each of these factors, early life health adversity continued to be statistically significantly associated with offspring anxiety disorders; general ELA ($Wald = 4.507$, $df = 1$, $p = .034$, $Exp(B) = 1.167$, 95% CI [1.012, 1.345]), current health status ($Wald = 4.036$, $df = 1$, $p = .045$, $Exp(B) = 1.157$, 95% CI [1.004, 1.333]). While not the focus of this study, post hoc main effect logistic regression analyses revealed that more traditionally conceptualized forms of ELA were statistically significantly associated with later depressive disorders ($Wald = 5.220$, $df = 1$, $p = .022$, $Exp(B) = 1.182$, 95% CI [1.024, 1.364]), but not anxiety disorders ($Wald = 1.723$, $df = 1$, $p = .189$, $Exp(B) = 1.105$, 95% CI [.952, 1.282]) in this sample.

Our second hypothesis was that the relationship between early life health adversity and internalizing disorders across adolescence would be attenuated among youth with high-quality family relationships, close friendships, and social lives. As presented in Tables 3 and 4, and in contrast to our hypothesis, none of the examined social relationships assessed at age 15 (family relationships, close friendships, and social life) emerged as statistically significant moderators of the relationship between early life health adversity and internalizing disorders. All interactions between early life health adversity and social relationships were null, failing to provide evidence for social relationships as protective factors in this sample.

Table 1. Demographic and descriptive characteristic

	N (%) or Range	*M (SD)*
Youth sex, female	363 (51.5)	
Youth ethnicity		
Aboriginal	14 (2.0)	
Maori/Islander	14 (2.0)	
Asian	33 (4.7)	
White	644 (91.3)	
Parental education		
Started secondary school or below	44 (6.2)	
Completed grade 10	336 (47.7)	
Completed grade 12	100 (14.2)	
College	180 (25.5)	
University	41 (5.8)	
Maternal depressive disorder by youth age 15, yes	295 (41.8)	
Early life health adversity	0 – 6	1.23 (1.22)
General early life adversity	0 – 4	1.31 (1.22)
Current health status at age 20	1 – 4.5	2.31 (.57)
Relationship quality at age 15		
Family	1 – 5	2.33 (.56)
Close friendship	1 – 5	2.21 (.48)
Social life	1 – 4.5	2.29 (.48)
Youth depressive disorder between ages 15 and 20, yes	191 (27.1)	
Youth anxiety disorder between ages 15 and 20, yes	168 (23.8)	

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Table 2. Correlations between key study variables

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Parent Education	–									
2. Early Life Health Adversity	−.068	–								
3. General Early Life Adversity	**−0.114**	**0.197**	–							
4. Maternal Depression Through Youth Age 15	.004	**0.126**	**0.232**	–						
5. Youth Depressive Disorder Diagnosis Ages 15 – 20	.007	**.087**	**0.104**	**.098**	–					
6. Youth Anxiety Disorder Diagnosis Ages 15 – 20	**−0.104**	**0.111**	**.090**	**0.133**	**0.303**	–				
7. Current Health Status Age 20	−.062	**0.137**	**.075**	**.080**	**0.209**	**0.102**	–			
8. Family Relationship Quality Age 15[1]	−.056	**0.102**	**0.194**	**0.204**	**0.169**	**0.183**	**0.164**	–		
9. Close Friendship Quality Age 15[1]	−.059	.064	.067	**.094**	.043	.040	−.010	**0.159**	–	
10. Social Life Quality Age 15[1]	.015	**.089**	.066	.073	**.082**	.048	.027	**.205**	**.509**	–

Note. Bolded value indicate correlation is significant at the 0.05 level or below. [1]Higher scores indicate lower quality relationships.

Table 3. Logistic regression of early life health adversity (ELHA) and offspring depressive disorders from 15 to 20 years of age

	N	*df*	*Wald*	*p*	*Exp (B)*	95% CI for *Exp (B)*	
						Lower	Upper
Main effect of ELHA	**701**	**1**	**4.935**	**.026**	**1.167**	**1.018**	**1.337**
Accounting for general early life adversity	693	1	3.115	.078	1.134	0.986	1.303
Accounting for current health status at age 20	701	1	2.082	0.149	1.110	0.963	1.279
Social relationships at age 15[1]							
Family relationships	**700**	**1**	**14.521**	**<.001**	**1.810**	**1.334**	**2.457**
Close friendships	700	1	1.352	.245	1.227	0.869	1.732
Social life	700	1	3.309	.069	1.378	0.975	1.947
ELHA * family relationships	700	1	1.441	.230	1.162	0.909	1.484
ELHA * close friendships	700	1	.007	.932	.990	.779	1.257
ELHA * social life	700	1	.350	.554	1.091	0.818	1.454
Potential effect moderators							
ELHA * offspring biological sex	701		.044	0.834	0.970	0.729	1.290
ELHA * maternal depression through offspring age 15	**701**	**1**	**6.697**	**.010**	**1.454**	**1.095**	**1.931**
Accounting for general early life adversity[2]	**693**	**1**	**6.553**	**.010**	**1.451**	**1.091**	**1.930**
Accounting for current health status at age 20[2]	**701**	**1**	**4.204**	**.040**	**1.355**	**1.013**	**1.811**

Note: Bolded values indicate significance, $p < 0.05$. [1]Higher scores indicate lower quality relationships. [2]Post-hoc analyses.

Our third hypothesis was to explore whether youth biological sex and maternal depression modified the association between early life health adversity and internalizing disorders later in development. As presented in Tables 3 and 4, biological sex did not emerge as a statistically significant moderator for either depressive or anxiety disorders, suggesting that the relationship between early life health adversity and later internalizing disorders does not differ by biological sex. Interestingly, differential results emerged for depressive and anxiety disorders with respect to the moderating role of maternal depression status. Maternal depression did not statistically significantly interact with early life health adversity to predict offspring anxiety disorders. However, the relationship between early life health adversity and offspring depressive disorders was statistically significantly moderated by maternal depressive status. Post hoc logistic regression analyses were undertaken to probe the direction of this interaction. These analyses demonstrated that early life health adversity was statistically significantly associated with offspring depressive disorders in the offspring of mothers who themselves had a history of depression ($Wald = 10.692$, $df = 1$, $p = .001$, $Exp(B) = 1.379$, 95% CI [1.137, 1.671]), but not in the offspring of mothers who did not have a history of depression ($Wald = .131$, $df = 1$, $p = .718$, $Exp(B) = .962$, 95% CI [0.781, 1.185]). In light of these

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Table 4. Logistic regression of early life health adversity (ELHA) and offspring anxiety disorders from 15-20 years of age

	N	*df*	*Wald*	*p*	*Exp (B)*	95% CI for *Exp (B)*	
						Lower	Upper
Main effect of ELHA	**701**	**1**	**5.420**	**.020**	**1.180**	**1.027**	**1.357**
Accounting for general early life adversity	**693**	**1**	**4.507**	**.034**	**1.167**	**1.012**	**1.345**
Accounting for current health status at age 20	**701**	**1**	**4.036**	**.045**	**1.157**	**1.004**	**1.333**
Social relationships at age 15[1]							
Family relationships	**700**	**1**	**13.174**	**< .001**	**1.781**	**1.304**	**2.433**
Close friendships	700	1	.660	.417	1.158	0.813	1.648
Social life	700	1	0.973	.324	1.196	0.838	1.709
ELHA * family relationships	700	1	.007	0.936	0.990	0.777	1.261
ELHA * close friendships	700	1	.122	.727	1.044	0.819	1.331
ELHA * social life	700	1	.008	0.929	0.987	0.734	1.325
Potential effect moderators							
ELHA * offspring biological sex	701	1	1.143	.285	0.854	.639	1.141
ELHA * maternal depression through offspring age 15	701	1	1.361	.243	1.185	0.891	1.575

Note: Bolded values indicate significance, $p < 0.05$. [1]Higher scores indicate lower quality relationships.

statistically significant moderator findings, we also examined whether maternal depression continued to be a statistically significant moderator between early life health adversity and offspring depressive disorders when independently accounting for (a) more traditionally conceptualized forms of ELA and (b) current health status at age 20. As detailed in Table 3, maternal depression continued to interact with early life health adversity to predict offspring depressive disorders when each of these variables was included in the model.

Discussion

This study demonstrates the potential legacy of health problems experienced early in life. To our knowledge, this is the first study to use a composite measure of adverse health experiences from birth through five years of age to predict both anxiety and depressive disorders in adolescence and early adulthood. Youth who experienced early life health adversity were more likely to meet diagnostic criteria for a depressive or anxiety disorder between 15 and 20 years of age, up to two decades following exposure. Furthermore, this pattern held for both males and females, suggesting that early health problems may increase risk for negative mental health outcomes regardless of biological sex. In other words, although females experience rates of depressive and anxiety disorders at approximately twice the rates of males (Altemus et al., 2014), females in this study were not uniquely sensitive to the long-lasting effects of early life health adversity. While a large body of literature has highlighted the robust association between more traditionally conceptualized forms of childhood adversity (e.g., socioeconomic disadvantage, parental divorce) and detrimental mental health outcomes (Bomysoad & Francis, 2020), this study suggests a unique and important role of early life health adversity.

Perhaps the most significant contribution of this study is illuminating the particularly potent association between early life health adversity and anxiety disorders in adolescence and early adulthood. After accounting for more traditionally conceptualized forms of adversity, early life health adversity continued to demonstrate prospective associations with anxiety disorders between 15 and 20 years of age. In fact, only early life health adversity – and not traditionally conceptualized forms of adversity – was associated with later anxiety disorders in this sample. This suggests a unique contribution to anxiety disorders associated with health problems throughout infancy and early childhood, as opposed to financial hardship, maternal stressful life events, parental discord, and parental separation occurring during this same developmental period. In the context of previous reports, the lack of an association between more traditionally conceptualized forms of adversity and anxiety disorders is somewhat surprising. For example, a nationally representative study of 29,617 U.S. youth between 12 and 17 years documented a graded association between adverse childhood experiences and adolescent psychiatric conditions, including but not limited to anxiety disorders (Bomysoad & Francis, 2020). Although this previous study examined a greater breadth of adverse exposures, the two most prevalent were parental divorce and economic hardship, which were included in the current study. Compared to those with no adverse childhood experiences, youth with one adverse childhood experience were twice as likely to have been diagnosed with an anxiety disorder; for youth with four or more adverse childhood experiences, this risk jumped to more than fivefold (Bomysoad & Francis, 2020). However, studies examining the relationship between early adversity and subsequent internalizing problems have often been retrospective in nature, with few accounting for risk and protective factors during adolescence. Recent literature suggests that more proximal factors may have greater impacts on adolescent mental health than adversity experienced early in life and that our results are not so anomalous (Gajos et al., 2022). Interestingly, our results suggest a different– and persistent– relationship between early life health adversity and anxiety disorders. While previous literature has offered ongoing health problems or activity limitations (i.e., proximal factors) as an explanation for the relationship between

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childhood health problems and subsequent psychopathology (Adams et al., 2019; Goodwin et al., 2013), our findings held even after accounting for current health status at age 20. Due to the design of the larger study, we were unfortunately not able to account for health adversity nor more traditionally conceptualized forms of adversity throughout childhood and early adolescence. However, the present findings suggest that the first few years of life may act as a sensitive developmental period for exposure to health problems. In other words, children who experience early life health adversity, regardless of later physical health functioning, may be more likely to subsequently develop anxiety disorders.

The general childhood adversity literature suggests several biopsychosocial mechanisms that may underlie the relationship between early life health adversity and later anxiety disorders (McLaughlin et al., 2019). For example, it is possible that children exposed to early life health adversity develop threat-related information processing biases, predisposing them for anxiety disorders (Briggs-Gowan et al., 2016; Shackman et al., 2007). In other words, repeated disruptions in homeostasis, a lack of predictability or controllability of bodily functions, and/or frequent encounters with the medical system may render youth ill-equipped to distinguish between threatening and safe environments (McLaughlin et al., 2019). Additionally, children who are exposed to threat or deprivation early in life tend to demonstrate heightened emotional reactivity and challenges with emotional regulation, which may predispose them to developing psychiatric disorders, including anxiety disorders (McLaughlin et al., 2019). Childhood health problems have, to-date, largely been left out of the general ELA literature, which tends to focus on the same key experiences of threat (e.g., maltreatment, violence) and deprivation (e.g., neglect, institutional rearing, socioeconomic disadvantage). However, early life health adversity may be characterized by both threat (e.g., harm to bodily integrity, repeated physical pain) and deprivation (e.g., prolonged hospitalization, missed opportunities for socialization) and thus may similarly engender lasting differences in fear learning, reward learning, and their underlying neurobiology (McLaughlin et al., 2019).

Future research is needed to determine both the shared and unique mechanisms, across multiple levels of analysis, that link early life health adversity—as opposed to more traditionally conceptualized adversity—with later anxiety disorders. For example, premature infants who experience pain while spending their early life in the Neonatal Intensive Care Unit tend to have long-lasting changes in pain sensitivity and cortisol responses, as well as elevated rates of psychiatric disorders (Victoria & Murphy, 2016). Animal research has identified permanent dysregulations in hypothalamic pituitary adrenal axis functioning and endogenous pain control following neonatal inflammatory pain, which are associated with changes in response to stress and anxiety later in development (Victoria & Murphy, 2016). This is just one example of how health adversity early in life could potentially induce physiological changes that prime youth to develop anxiety disorders. From a cognitive perspective, it is also possible that early health problems could result in heightened attention toward physiological sensations, which could be adaptive at times yet also induce hypervigilance and elevated anxiety. At the social level, it is important to consider the role of caregiving experiences and behaviors that may increase risk for the development of youth anxiety. For example, while sensitive and responsive parenting is known to protect youth from anxiety disorders (Cooke et al., 2022), one study recently reported nearly universal relational difficulties among infants with complex congenital heart disease and their mothers (Tesson et al., 2024). Beyond infancy, growing literature emphasizes the importance of parent–child health communication, such as reminiscing about past pain experiences, in predicting subsequent pain and fear (Noel et al., 2019). Parental accommodation is known to be one of the greatest influences on child anxiety (Lebowitz et al., 2013), and this may be especially nuanced in youth who experience early life health adversity. For example, although it remains to be studied empirically, it is easy to imagine how a caregiver of a child with complex healthcare demands may be reluctant to ever separate from their child, and that the child may then experience separation anxiety, having learned that the world is not safe without their caregivers' physical presence. Importantly, while this study aimed to distinguish early life health adversity from traditionally conceptualized adverse childhood experiences, it is also important to remember the vast heterogeneity *within* early life health adversity (e.g., prematurity, traumatic brain injury, and persistent asthma) and to continue to examine patterns of both equifinality and multifinality that likely stem from those experiences (Cicchetti & Rogosch, 1996).

Interestingly, from a statistical significance standpoint, divergent patterns emerged when looking at depressive disorders. First, while we must acknowledge similar effect sizes and overlapping confidence intervals with anxiety disorders, the main effect of early life health adversity on depressive disorders at ages 15 to 20 was no longer statistically significant after independently controlling for ELA as traditionally conceptualized, as well as current health status in early adulthood. This suggests that both general forms of ELA and more proximal physical health problems may be more salient for predicting depressive disorders than early life health adversity per se. However, maternal depression moderated this relationship. Specifically, early life health adversity increased risk for depressive disorders, but only in youth who were exposed to maternal depression by 15 years of age. This suggests that maternal depression may be related to early life health adversity in a diathesis-stress fashion, such that it predisposes youth—through both genetic and environmental processes—to be susceptible to the adverse effects of early life health adversity and thus more likely to develop depressive disorders (Burke & Elliott, 1999; Goodman, 2020; Heim & Nemeroff, 1999). Given the robust research linking maternal depression to higher levels of a wide range of psychiatric disorders (Goodman et al., 2011), as well as the shared genetic risks across anxiety and depressive disorders (Kalin, 2020), the specificity of the interaction between early life health adversity and maternal depression in predicting youth depressive, but not anxiety disorders, is noteworthy. It will be important for future studies to examine relationships between early childhood health problems and maternal depression, as well as potential mechanisms underlying these relationships, such as parenting behaviors (Goodman & Garber, 2017). For example, it is possible that early life health problems in a child exacerbate a mother's depression, leading to decreased help-seeking within medical systems and further child health problems (Minkovitz et al., 2005, Perry, 2008; Raposa et al., 2014). Depression may also influence how a woman communicates with her child about physical illness, which could potentially engender maladaptive illness cognitions within a child, setting the stage for depressive disorders (Lim et al., 2011; Rodriguez et al., 2013; Verhoof et al., 2014). Parenting a young child with complex healthcare needs requires significant emotional and financial commitments; these added burdens may be particularly difficult and costly in the context of maternal depression, having a cascade of effects on the entire family unit

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and potentially setting the stage for offspring depressive disorders (Ferro & Boyle, 2015).

In contrast to our hypothesis, none of the social relationships we examined emerged as protective factors in the relationship between early life health adversity and later internalizing disorders. While high-quality family relationships, close friendships, and broader peer functioning are certainly important in adolescence, our results suggest that they are not enough to "undo" the detrimental effects of early life health adversity on mental health outcomes. Due to our study design, we examined social relationships at age 15. It is possible that we would have attained differential results had we examined social relationships earlier in development, such as attachment relationships emerging in infancy or peer relationships throughout childhood and pre-adolescence. It is also possible that measures at concurrent time points (e.g., social relationships from ages 15 – 20 years, assessed concurrently with mental health) may be more closely linked to internalizing disorders. Our null findings underscore the importance of examining a broader range of protective factors across ecological systems (e.g., individual, dyad, school, healthcare system, and culture) and time among youth who experience health problems (Hilliard et al., 2015; Masten et al., 2021).

This study involved secondary data analysis of a larger investigation of mental health in mother–child dyads. This brought some inherent limitations, as the larger study was not designed for the purposes of examining early life health adversity. For example, while we had robust information regarding early life health adversity, it would have been ideal to follow the developmental trajectories of early life health problems with repeated measures throughout childhood and adolescence. This information is critical to determining whether early life represents a sensitive developmental period whereby health adversity exerts particularly salient effects on adolescent and young adult internalizing disorders, or whether it is that children who experience early life health adversity are more likely to continue experiencing health adversity throughout childhood and adolescence. We addressed this limitation to the best of our ability by assessing health adversity over the past several months at age 20, via a comprehensive interview, yet this does not capture health through much of development.

Our composite measure of early life health adversity builds upon previous research with this sample (Dalton et al., 2016; Raposa et al., 2014). It is also an important first step toward establishing the importance of the general construct of early life health adversity, as opposed to focusing on specific conditions like a chronic illness or prematurity, as much of the previous literature has relied on. However, our index lacks specificity, and it is possible that different types of health adversity exert differential effects. We also did not have access to medical records, which would have been ideal to corroborate maternal reports of early life health adversity.

Our sample lacked racial and ethnic diversity, thus limiting the generalizability of our results. Additionally, Australia has universal healthcare insurance, so generalizability to countries that do not have national healthcare coverage is unclear. While it was a major strength to examine traditionally conceptualized forms of adversity in addition to health adversity, we did not focus on several important forms of ELA, including abuse and neglect. Our study was also limited by focusing exclusively on diagnostic outcomes, and on broad classes of internalizing disorders in particular. In order to gain a more comprehensive understanding of the long-term impacts of early life health adversity on psychopathology, future studies should consider examining specific anxiety and depressive disorders and subclinical symptoms, as well as expanding to focus on externalizing disorders.

Notably, our relatively large sample size and prospective, longitudinal design spanning 20 years represent significant strengths. Furthermore, measures were collected across multiple timepoints, with a focus on potential sensitive periods and developmental transitions—infancy, early childhood, adolescence, and early adulthood. Anxiety and depressive disorders, as well as current health status and social relationship qualities, were all assessed via gold-standard comprehensive interviews. These factors set our study apart from much of the existing literature on childhood health problems and subsequent psychiatric problems, which is often reliant on self-report measures and cross-sectional or retrospective in nature. Overall, this study demonstrates the importance of early life health adversity in influencing adolescent and young adult mental health and lays the groundwork for future research in this area.

Conclusions

In sum, we found that early life health adversity was associated with increased risk for internalizing disorders present in the transition from adolescence to adulthood, with unique associations found for anxiety and depressive disorders. While there is a plethora of literature on the relationship between *general* ELA and subsequent psychiatric disorders, early life *health* adversity is typically left out of this research. This study suggests that an expanded conceptualization of ELA—that includes childhood health problems—may be warranted. Future research would benefit from exploring the developmental trajectories of health adversity and anxiety disorders, as well as refining this relationship by examining particular types of health adversities and particular types of anxiety disorders. Understanding these trajectories may allow for early intervention and prevention efforts. Additionally, dual exposure to maternal depression and early life health adversity appears to generate a unique risk for the development of depressive disorders. Routine mental health screenings may be warranted for youth who experience early life health adversity, as well as their mothers. Pediatric primary care may be an ideal setting for early screening, prevention, and intervention efforts.

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Competing interests. None.

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